Amendments to the Claims

The listing of claims will replace all prior versions and listings of claims in the application.

Claim 1 (currently amended): A method for increasing the level of a therapeutic gene product in a subject, the method comprising administering to said subject

(a) a first viral vector comprising a therapeutic nucleic acid encoding said therapeutic gene product, wherein said therapeutic gene product is expressed through operable linkage of said nucleic acid to a promoter, which functions in hepatocytes, and

(b) an agent that reduces Kupffer cell function, wherein said agent is a second viral vector that does not comprise said therapeutic nucleic acid;

wherein said second viral vector is the same type as said first viral vector;

wherein said agent is administered prior to or concurrently with administration of said first viral vector; ~~except that if said agent is identical to said first viral vector, then said agent is administered prior to said first viral vector; and~~

wherein said agent is administered by a route selected from the group consisting of direct administration to the liver, intravenous administration, or intraperitoneal administration;

wherein said first viral vector and said agent reach the liver following administration; and

wherein levels of said therapeutic gene product are increased by administration of said agent.

Claims 2 - 33 (canceled).

Claim 34 (currently amended): A method for increasing the level of a therapeutic gene product in a subject, the method comprising administering to said subject

(a) a first viral vector comprising a therapeutic nucleic acid encoding said therapeutic gene product, wherein said therapeutic gene product is expressed through operable linkage of said nucleic acid to a promoter, which functions in hepatocytes, and

(b) an agent that reduces Kupffer cell function, wherein said agent is a second viral vector;

wherein said second viral vector is the same type as said first viral vector;

wherein said agent is administered prior to, but less than 1 hour prior to, administering said first viral vector; ~~except that if said agent is identical to said viral vector, then said agent is not administered concurrently with said viral vector; and~~

wherein said agent is administered by a route selected from the group consisting of direct administration to the liver, intravenous administration, or intraperitoneal administration;

wherein said first viral vector and said agent reach the liver following administration; and

wherein levels of said therapeutic gene product are increased by administration of said agent.

Claim 35 (currently amended): The method according to claim 34, wherein said agent is administered less than five minutes prior to administering said first viral vector.

Claim 36-37 (canceled).

Claim 38 (currently amended): The method according to claim 1, wherein said first ~~and/or~~ and second viral vectors are ~~vector is an~~ adenovirus vectors ~~vector~~.

Claim 39 (currently amended): The method according to any one of claims 34-35 ~~38~~, wherein said first and second viral vectors are ~~vector is an~~ adenovirus vectors ~~vector~~.

Claim 40 (canceled).

Claim 41 (currently amended): The method according to any one of claims 1, ~~or~~ 34-35, or 38, wherein said subject is a primate.

Claim 42 (previously presented): The method according to claim 41, wherein said primate is a human.

Claim 43 (canceled).

Claim 44 (currently amended): The method according to any one of claims 1 or 34-35 ~~37~~, wherein said first viral vector is administered by a route selected from the group consisting of oral administration, nasal administration, parenteral administration, transdermal administration, intrabronchial administration, intraperitoneal administration, direct injection into cells, tissue, organ or tumor, intravenous administration, subcutaneous administration, and intramuscular administration.

Claim 45 (canceled).

Claim 46 (currently amended): The method according to any one of claims 1 or 34-35 ~~37~~, wherein said first and second viral vectors are ~~vector is a~~ replication-defective viral vectors ~~vector~~.

Claim 47-51 (canceled).

Claim 52 (currently amended): A pharmaceutical composition comprising

(a) a first viral vector, wherein said vector comprises a therapeutic nucleic acid encoding a therapeutic gene product expressed through operable linkage of said nucleic acid to a promoter, which functions in hepatocytes,

(b) an agent that reduces Kupffer cell function, ~~wherein said agent is not identical to said viral~~ wherein said agent is a second viral vector that does not comprise said therapeutic nucleic acid,

wherein said second viral vector is the same type as said first viral vector;

and

(c) a pharmaceutically acceptable carrier;

wherein said first viral vector and said agent are not conjugated.

Claim 53 (currently amended): The pharmaceutical composition according to claim 52, wherein said first and second viral vectors are ~~vector is~~ provided in ~~a~~ viral particles ~~particle~~.

Claim 54 (canceled).

Claim 55 (new): The pharmaceutical composition according to claim 52, wherein said first and second viral vectors are adenovirus vectors.

Claim 56 (new): The method according to claim 1, wherein said agent is administered less than 24 hours prior to administration of said first viral vector.

Claim 57 (new): The method according to claim 1, wherein said agent is administered concurrently with administration of said first viral vector.

Claim 58 (new): A method for increasing the level of a therapeutic gene product in a subject, the method comprising administering to said subject

(a) a first viral vector comprising a therapeutic nucleic acid encoding said therapeutic gene product, wherein said therapeutic gene product is expressed through operable linkage of said nucleic acid to a promoter, which functions in hepatocytes, and

(b) an agent that reduces Kupffer cell function, wherein said agent is a liposome-encapsulated cytotoxin;

wherein said agent is administered less than 24 hours prior to or concurrently with administration of said first viral vector;

wherein said agent is administered by a route selected from the group consisting of direct administration to the liver, intravenous administration, or intraperitoneal administration;

wherein said first viral vector and said agent reach the liver following administration; and

wherein levels of said therapeutic gene product are increased by administration of said agent.

Claim 59 (new): The method according to claim 58, wherein said agent is administered less than one hour prior to administering said first viral vector.

Claim 60 (new): The method according to claim 58, wherein said first viral vector is an adenovirus vector.

Claim 61 (new): The method according to claim 58, wherein said subject is a primate.

Claim 62 (new): The method according to claim 61, wherein said primate is a human.

Claim 63 (new): The method according to claim 58, wherein said first viral vector is administered by a route selected from the group consisting of oral administration, nasal administration, parenteral administration, transdermal administration, intrabronchial administration, intraperitoneal administration, direct

injection into cells, tissue, organ or tumor, intravenous administration, subcutaneous administration, and intramuscular administration.

Claim 64 (new): The method according to claim 58, wherein said first viral vector is a replication-defective viral vector.

Claim 67 (new): The method according to claim 58, wherein said liposome-encapsulated cytotoxin is liposome-encapsulated doxorubicin.

Claim 68 (new): A pharmaceutical composition comprising

(a) a first viral vector, wherein said vector comprises a therapeutic nucleic acid encoding a therapeutic gene product expressed through operable linkage of said nucleic acid to a promoter, which functions in hepatocytes,

(b) an agent that reduces Kupffer cell function, wherein said agent is a liposome-encapsulated cytotoxin,

and

(c) a pharmaceutically acceptable carrier.